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Steinfl + Bruno LLP
155 N. Lake Ave. Ste 700
Pasadena, CA 91101

EXAMINER
BORIN, MICHAEL L

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE PATENT TRIAL AND APPEAL BOARD

Ex parte WILLIAM A. GODDARD III, RAVINDER ABROL, ISMET C. TANRIKULU, and ADAM R. GRIFFITH

Appeal 2017-000560[1]
Application 12/944,700
Technology Center 1600

Before RICHARD M. LEBOVITZ, DAVID COTTA, and TAWEN CHANG, *Administrative Patent Judges*.

LEBOVITZ, *Administrative Patent Judge*.

DECISION ON APPEAL

This appeal involves claims directed to computer-operated methods for predicting binding poses of a binding molecule to a target molecule. The Examiner rejected the claims under 35 U.S.C. § 103 as obvious and under 35 U.S.C. § 101 as directed to a judicial exception to patent eligibility. We have jurisdiction under 35 U.S.C. § 6(b). The rejections are affirmed.

STATEMENT OF THE CASE

Appellants appeal from the Examiner's rejection of claims 1–5 and 8–23. The claims stand rejected as follows:

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[1] The Appeal Brief ("Appeal Br.") 2 lists California Institute of Technology as the assignee and real-party-in-interest.

1. Claim 1–5, 8–10, 18, 19, and 21–23 under 35 U.S.C. § 103(a) as obvious in view of Cho et al. (Art E. Cho et al. , *The MPSim-Dock Hierarchical Docking Algorithm: Application to the Eight Trypsin Inhibitor Cocrystals*, 26 J. OF COMPUT CHEM 48, 48–71 (2005) ("hereinafter "Cho")), Itai et al. (US 2006/0100789 A1, published May 11, 2006 (hereinafter "Itai")), and McConkey et al. (Brendan J. McConkey et al., *The Performance of Current Methods in Ligand-Protein Docking*, 83 CURRENT SCIENCE No. 7, 845, 845–856 (2002) (hereinafter "McConkey")). Final Office Action ("Final Act.") 7.

2. Claims 11–20 under 35 U.S.C. § 103(a) as obvious in view of Cho, Itai, McConkey, and Hellinga et al. (US 2004/0229290 A1, published Nov. 18, 2004 (hereinafter "Hellinga")). *Id.* at 11, 13.

3. Claims 1–5 and 8–23 under 35 U.S.C. § 101 as directed to patent ineligible subject matter. *Id.* at 3.

Claim 1 is representative and reads as follows:

> 1. A computer-operated method for predicting binding poses of a binding molecule, wherein the binding molecule is adapted to be bound to a target molecule, the method comprising the following computer-operated steps wherein a computer performs the steps in single-processor mode or multiple-processor mode:
>
> providing at least one molecular pose for the binding molecule;
>
> clustering the at least one molecular pose into at least one family, wherein the clustering is based on position of each molecular conformation in the target molecule;
>
> selecting, upon completion of all iterations of the providing and the clustering, a family head for each family in the at least one family based on geometric properties;

selecting a full set or subset of families based on interaction energy between each family head and the target molecule; and

selecting a full set or subset of molecular poses from among the molecular poses in the full set or subset of families based on interaction energy between each molecular pose and the target molecule;

wherein the interaction energy comprises total interaction energy, polar interaction energy, and phobic interaction energy and the molecular pose selecting comprises:

selecting a first set of molecular poses from among the molecular poses in the full set or subset of families based on the total interaction energy;

selecting a second set of molecular poses from among the molecular poses in the full set or subset of families based on the polar interaction energy; and

selecting a third set of molecular poses from among the molecular poses in the full set or subset of families based on the phobic interaction energy.

THE PERSON OF ORDINARY SKILL IN THE ART

When making a patentability determination under 35 U.S.C., we consider the claims and the scope and content of the prior art to be directed to one of ordinary skill in the art. Thus, a determination as to whether the claims conform to the patentability requirements of 35 U.S.C. is made from the perspective of one of ordinary skill in the art. In this case, the claimed subject matter involves computer operated methods to predict binding poses of a binding molecule to a target molecule. The method has steps of selecting poses based on interaction energies and involves computer modeling. The cited prior art includes patents, published patent applications, and scientific journal articles in the fields of computer-aided methods for the identification and characterization of ligand-protein interactions and energy

scoring algorithms. Persons who publish in scientific journals typically are scientists who have advanced degrees in the pertinent field (e.g., chemistry, biology), such as masters and Ph.D. degrees. Accordingly, the person of ordinary skill in the art pertinent to the claimed subject matter is a scientist, familiar with the patent and scientific literature, who has (1) at least an advanced degree in chemistry or biology and (2) experience in computer protein-ligand modeling, determining energy interactions between molecules, and performing energy computations. Such ordinary skilled worker would have studied the interactions between proteins and ligands, i.e., binding of molecules to targets.

OBVIOUSNESS REJECTION

Claim 1 is directed to a computer-operated method for predicting binding poses of a binding molecule bound to a target molecule. A "pose" is described in the Specification as a molecular "conformation" that takes place when a binding molecule binds to the target molecule, such as when a ligand binds to a protein. Spec. ¶ 3. The claimed method involves steps of providing molecular poses for the binding molecule and clustering the poses based "on position of each molecular conformation in the target molecule." The poses are clustered into at least one family. "A full set or subset of molecular poses" is selected "based on *interaction energy* between each molecular pose and the target molecule." Appeal. Br., Claims App. (emphasis added).

The interaction energy of the claims comprises: 1) total interaction energy, 2) polar interaction energy, and 3) phobic interaction energy.

The molecular pose selecting comprises:

A) "selecting a first set of molecular poses . . . based on the *total interaction energy*;"

B) "selecting a second set of molecular poses . . . based on the *polar interaction energy*;" and

C) "selecting a third set of molecular poses . . . based on the *phobic interaction energy*."

The Specification defines total interaction energy as

> a sum of vaccum [sic] energy of the binding molecule and nonbond energy between the binding molecule and the target molecule; polar interaction energy, which is the polar component of the total interaction energy; and phobic interaction energy, which is the hydrophobic component of the total interaction energy. Nonbond energy refers to the sum of Coulomb, van der Waals, and hydrogen-bond energies.

Spec. ¶ 47.

The Examiner found that Cho describes the same steps of claim 1 of providing molecular poses and clustering the poses into families. Final Act. 8. The Examiner found that Cho teaches calculations of A) total interaction energy, but not selecting poses based on the individual energy components as in the claim, i.e., B) and C). *Id.* at 9. However, the Examiner found it would have been obvious to have selected poses based on the interaction energy of interest. As evidence, the Examiner cited the Itai and McConkey publications describing hydrogen bonding, van der Waals, electrostatic, and hydrophobic interactions as important interactions in stable binding between ligands and target molecules and to create scoring functions. *Id.*

Appellants contend that there is no teaching or suggestion in the cited publications to perform all three selections (A, B, and C above) to select molecular poses. Appeal Br. 22.

Findings of Fact ("FF")

We begin with the most pertinent facts.

Cho Publication

Cho discloses:

FF1.

> To help improve the accuracy of protein–ligand docking as a useful tool for drug discovery, we developed MPSim-Dock, which ensures a comprehensive sampling of diverse families of ligand conformations in the binding region followed by an enrichment of the good energy scoring families so that the energy scores of the sampled conformations can be reliably used to select the best conformation of the ligand.

Cho, Abstract.

FF2.

> We used the Dreiding all-atom FF for both the protein and the ligand. This includes the internal energy of the ligand along with the nonbond energy of interaction with the protein. The energy expression includes valence energies (bonds, angles, torsion, and inversion) and nonbond interactions (Coulomb, van der Waals, and hydrogen bond) within the ligand and with the protein.

Id. at 49 (footnote omitted).

Itai Publication

Itai discloses:

FF3.

> It is known from the crystallographic analyses of biopolymer-ligand molecule complexes that among these intermolecular interactions, hydrogen-bond, electrostatic and hydrophobic interactions and the like are particularly important. In drug design and structure-activity relationship study, it is very important to know whether a compound molecule can form a

> stable complex with its target biopolymer and, if so, what kind of binding mode the complex has (i.e., which functional group in the ligand-binding site of the biopolymer interact which functional groups in the ligand molecule in what kind of mode) and how stable the complex is.

Itai ¶ 4.

FF4.

> F. Jiang et al. developed an automatic docking method in which intermolecular interactions such as hydrogen-bond, electrostatic interaction and the like are considered qualitatively in addition to the shape complementarity which Kuntz et al. highlighted (F. Jiang and S. Kim, J. Mol. Biol. 219, 79 (1991)).

Id. ¶ 10.

FF5.

> As a result of various studies, the inventors developed methods for docking automatically any ligand molecules to the ligand-binding sites in biopolymers by searching the binding modes of stable complexes and the active conformations of the ligand molecules at the same time by taking into account hydrogen-bond, electrostatic interaction and van der Waals force as the interactions between the biopolymers and the ligand molecules, and they succeeded in solving the above-mentioned problems.

Id. ¶ 14.

FF6.

> Thus, all possible combinations of the hydrogen-bonds formed by the biopolymer and ligand molecule are selected and thereby the mode of binding of the ligand molecule to the biopolymer can be searched systematically and efficiently.

Id. ¶ 74.

FF7.

> The intermolecular interaction energy between the biopolymer and the hydrogen-bonding part of the ligand molecule (E_{inter}) can be calculated by the following formula:
>
> $$E_{inter} = \sum_{k} (G_{vdw}(k) + G_{elc}(k) \cdot q_k)$$
>
> where G_{vdw} (k) is the van der Waals interaction energy of atom k, G_{elc} (k) is the electrostatic interaction energy of atom k and q_k is the atomic charge on atom k.

Id. ¶ 99

McConkey Publication

McConkey discloses:

FF8.

> The most common means of estimating a binding affinity to be used as a scoring function is by partitioning of the free energy into recognizable components. The number and type of terms vary between scoring functions, but in general there are terms for hydrogen bonding, van der Waals, electrostatic and hydrophobic interactions, and entropy penalties.

McConkey 847.

FF9.

"The weighting of each of the interaction terms is estimated by fitting a regression model to a test set of ligand-protein complexes with known binding affinities." *Id.* at 848.

FF10.

> The scoring function in GOLD is an energy partition function, with terms for hydrogen bonding, ligand-protein interactions and the internal energy of the ligand. Multiple atom types were used to calculate hydrogen bond energies between donor and acceptor pairs. . . . The internal energy of the ligand was calculated using a 6-12 van der Waals potential and the Tripos force field. The scoring function accounts for the desolvation of polar residues, but does not address desolvation or lipophilic interactions

> explicitly. It was effective in identifying a top-ranked solution within 2 Å RMSD in approximately half the cases. After publication of the validation paper, recognition of hydrophobic-hydrophobic interactions was added to the algorithm and tested on an additional 34 ligands, and the data were published on the GOLD website.

Id. at 851–852 (footnote omitted).

FF11.

"There are inherent limits to some scoring approaches when used independently of other methods. The Poisson-Boltzmann equation, for example, can provide an accurate description of the electrostatic field around a protein, but if used alone does not account for desolvation or other interactions." *Id.* at 855.

FF12.

"Subtle changes in electrostatic properties can result in large changes in binding affinity within a given type of interaction. A scoring function that is a sum of pairwise additive terms also neglects non-additive behaviour between and among groups. Hydrophobic interactions are a good example of this." *Id.*

Discussion

Appellants' principal argument is that the claims are nonobvious in view of Cho, Itai, and McConkey because one of ordinary skill in the art would not have selected molecular poses for total-, polar-, phobic interaction energies individually, but rather would have utilized an energy scoring function that contain these as multiple terms for one calculation of total interaction energy. Appeal Br. 21–22. Appellants contend that the prior art teaches away from the claimed features because the prior art teaches utilizing *all* binding energies to determine the optimal binding poses. Reply

Br. 6. Appellants also argue that Itai teaches away utilizing phobic energy interactions for pose selections because, while Itai mentions phobic interactions in its Background section, Itai does not use the term in its actual calculations. Appeal Br. 21.

Appellants' arguments do not persuade us that the Examiner erred in determining that the claims are obvious in view of Cho, Itai, and McConkey.

The first pose selection criteria recited in the claim is selecting poses based on "total interaction energy." The definition in the Specification of "total interaction energy" includes Coulomb, van der Waals, hydrogen-bond energies, and hydrophobic energies. Spec. ¶ 47. These energy components appear to be the same energy components described in Cho (FF2), Itai (FF3, FF4, FF5), and McConkey (FF8, FF10) for determining total interaction action for selecting binding molecule poses. Thus, the first selection criteria recited in claim 1 used to select molecular poses is disclosed in or suggested by the teachings in Cho, Itai, and McConkey, which teach that total interaction energy is important in determining the binding between binding and target molecules.

The second and third pose selection criteria recited in the claim use polar and phobic energy interactions, respectively, to select binding poses. Appellants contend that one of ordinary skill in would not have used these criteria individually to select molecular poses.

We agree with the Examiner that there would have been reason to select poses based on polar and phobic energy interactions, individually.

The cited publications indicate that the persons of skill in the art were developing methods to improve energy scoring and identify parameters to improve it. FF1, FF3, FF4, FF5, FF10, FF11. One of ordinary skill in the

art who wanted to improve energy scoring for the purpose of modeling interactions between a binding molecule and its target would have sought to understand the individual contributions by each energy component when determining what poses to select.

For example, Itai describes prior docking programs in its background section. FF4. Itai characterizes its method as an improvement over the prior art by "taking into account hydrogen-bond, electrostatic interaction and van der Waals force as the interactions between the biopolymers and the ligand molecules." FF5. McConkey describes utilizing the GOLD energy scoring function that takes into account hydrogen bonding and van der Waals forces. FF10. McConkey teaches that the scoring function was subsequently improved by adding hydrophobic interactions to the scoring function. FF10. McConkey also acknowledges limitations to current scoring approaches. FF11. Thus, both publications indicate that the ordinary skilled worker sought to adjust the energy scoring function by adding energy interaction terms to improve its ability to pick the best poses between the binding and target molecules.

Itai also teaches selecting "all possible combinations of the hydrogen-bonds formed by the biopolymer and ligand molecule" to search for the mode of binding (FF6), providing a further reason to determine how hydrogen bonding (a polar bond energy interaction B as in the claims) influences the selection of binding poses.

McConkey teaches "estimating a binding affinity to be used as a scoring function . . . by partitioning of the free energy into recognizable components" (FF8) and weighting each of the interaction terms (FF9), thus also prompting one of ordinary skill in the art to look at the contribution of

the individual recognizable energy component when selecting molecular poses. McConkey further states that "[s]ubtle changes in electrostatic properties can result in large changes in binding affinity within a given type of interaction" (FF12), again providing the ordinary skilled worker with reason to evaluate the effect of individual energy interactions on binding poses.

Thus, based on these teachings, one of ordinary skill in the art, would have had reason to determine the individual energy contributions to the total interaction energy to determine how effective they are alone, and in combination with other energy interaction components, in selecting molecular poses.

For the foregoing reasons, Rejection 1 of claim 1 is affirmed. The same arguments were made for claim 21. Appeal Br. 19. Thus, the rejection of claim 21 is affirmed for the same reasons. Because separate arguments were not provided for claims 2–5, 8–10, 18, 19, and 21–23 (Rejection 1) and claims 11–20 (Rejection 2) (*Id.* at 23, 24), those claims fall with claims 1 and 21. 37 C.F.R. § 41.37(c)(1)(iv).

SECTION 101 REJECTION

The Examiner rejected the claims as directed to a judicial exception to patent eligibility under 35 U.S.C. § 101. Final Act. 2–3. The Examiner found that the claims are directed to an abstract idea performed on a computer to predict binding poses of a molecule to a target molecule, such as a receptor. *Id.* at 4. The Examiner stated the claimed steps are directed to "to data manipulation, which is an abstract construct, having no particular

concrete or tangible form" which do not add significantly more to the idea, itself. *Id.* at 5.

Appellants contend that the claims "are not dealing with something as abstract as 'economic value', nor are they dealing with claiming mathematical formulas or algorithms regarding numbers just as numbers in and of themselves – the algorithms of the instant claims are procedural method steps dealing with numbers representative of physical properties of objects (molecules)." Appeal Br. 10. Appellants contend that the steps are not "just 'data manipulation'" but can be used for rational drug design." *Id.* at 10–11. Appellants also state "that, seen as a whole, the claims present something significantly more than an abstract idea due to the claim's relationship to a technological art." *Id.* at 15. Appellants also contend that the claims "are not merely implementing conventional steps for 'predicting binding poses of a molecule binding to its receptor.'" *Id.* at 14. Specifically, Appellants contend that selecting molecular poses based on total interaction energy, polar interaction energy, and phobic interactions is not conventional. *Id.*

Discussion

The determination of patent eligibility under 35 U.S.C. § 101 is a two-step analysis. First, it must be determined whether the claims are directed to patent-ineligible concept, e.g., a law of nature, natural phenomenon, or abstract idea. *Alice Corp. Pty. Ltd. v. CLS Bank Int'l*, 134 S. Ct. 2347, 2355 (2014). Second, the elements of the claims, "both individually and as an ordered combination," are considered "to determine whether the additional elements transform the nature of the claim into a patent-eligible application of that abstract idea." *DDR Holdings, LLC v.*

Hotels.com, L.P., 773 F.3d 1245, 1255 (2014). "This second step is the search for an 'inventive concept,' or some element or combination of elements sufficient to ensure that the claim in practice amounts to 'significantly more' than a patent on an ineligible concept." *Id.* (quoting *Alice*, 134 S. Ct. at 2347).

The Federal Circuit acknowledges that it is difficult to discern when claims are directed to an abstract idea. *DDR Holdings*, 773 F.3d at 1255. Because of this difficulty, the courts have taken a case-by-case approach: "Instead of a definition, then, the decisional mechanism courts now apply is to examine earlier cases in which a similar or parallel descriptive nature can be seen—what prior cases were about, and which way they were decided." *Amdocs (Israel) Limited v. Openet Telecom, Inc.*, 841 F.3d 1288, 1294 (2016). In other words, the courts look to the similarities and differences with other claims subject to a patent eligibility analysis in earlier decided cases to determine whether the claims at issue are directed to subject matter eligible for a patent.

We thus must first decide whether the claim is directed to patent-ineligible subject matter. We begin with the purpose of claim 1.

Claim 1 is a "computer operated method for predicting binding poses of a binding molecule." The Specification teaches that the process can be used in rational drug design to design a drug to bind to a target molecule, such as a protein. Spec. ¶¶ 3, 7.

The claim begins with a step of providing at least one molecule pose for the binding molecule. As explained in the Specification, a molecular pose is conformation of a molecule, i.e., a shape or configuration of it in space. *Id.* ¶¶ 3, 32. The claim does not recite how the poses are determined,

but the Specification explains that poses can be generated utilizing a program, such as MacroModel. *Id.* ¶¶ 29, 30. Thus, a known algorithm can be used to produce the molecular poses.

The poses are clustered into families, "where a family is a group of molecular poses in the population of molecular poses that show similar positions (also known as orientations) with respect to the target molecule." *Id.* ¶ 34. The claims do not recite how the clustering is performed. However, the Specification teaches that "clustering (S 110) into families is based on RMSD (root mean square difference) calculations between any two molecular poses. Specifically, distance between two molecular poses is calculated by averaging deviation of the two poses over all heavy (non-hydrogen) atoms." *Id.* ¶ 36. Thus, clustering can be performed using a mathematical formula.

The claim further recites that molecular poses from the families are selected based on interaction energy between the pose and the target molecule. As discussed above, the selecting step is performed based on total-, polar-, and phobic interaction energies. Neither the claims nor the Specification explain how the interaction energy calculations are accomplished. Thus, any conventional way of calculating energies can be used. The Specification teaches that the interaction energies are used to pick the "best" binding poses. *Id.* ¶ 44.

In sum, all the recited steps in the claim utilize algorithms in determining poses, family clusters, and interaction energies. For this reason, we agree with the Examiner that the claims are directed to "data manipulation," where the data is the computer representations of the poses, clusters, and energies that are manipulated to select the best molecular poses.

We thus turn to the recent cases to determine whether the claimed subject matter is eligible for a patent under § 101.

In *Digitech Image Technologies, LLC v. Electronics for Imaging, Inc.*, 758 F.3d 1344, 1348 (2014), the claims were directed to "a process of taking two data sets and combining them into a single data set, the device profile. The two data sets are generated by taking existing information—*i.e.*, measured chromatic stimuli, spatial stimuli, and device response characteristic functions—and organizing this information into a new form." The court found that the method claims were drawn to "an abstract idea because it describes a process of organizing information through mathematical correlations and is not tied to a specific structure or machine." *Digitech,* 758 F.3d at 1350. Furthermore, the court held:

> The above claim thus recites an ineligible abstract process of gathering and combining data that does not require input from a physical device. As discussed above, the two data sets and the resulting device profile are ineligible subject matter. Without additional limitations, a process that employs mathematical algorithms to manipulate existing information to generate additional information is not patent eligible.

Id. at 1351.

The claims in this case are similar to *Digitech* because, while the algorithms to determine poses are performed on a computer using software, there is no input of data from a physical device, but rather the claim appears to solely involve the manipulation of data, beginning from data provided by a known computer program (MacroModel, Spec. ¶¶ 29, 30) that generates molecular poses.

The claims in this case are distinguishable from *McRO, Inc. v. Bandai Namco Games Am. Inc.*, 837 F.3d 1299, 1313 (Fed. Cir. 2016), which

involved computer automation "to produce accurate and realistic lip synchronization and facial expressions in animated characters" that previously could only be produced by human animators." In *McRO*, while the claims involved the manipulation of data, e.g., generating morph weight sets to animate lip and facial expressions of three dimensional characters, the court found that "the automation goes beyond merely 'organizing [existing] information into a new form' [as in *Digitech*] or carrying out a fundamental economic practice." *McRO*, 837 F.3d at 1315. Instead, the court found that the "claimed process uses a combined order of specific rules that renders information into a specific format that is then used and applied to create desired results: a sequence of synchronized, animated characters." *Id.*

The rejected claims in this case are different because the data is not used to produce a new result, such as the animation of characters in *McRO*, but rather the data is used to select poses from a family of clustered poses which are generated by a known and conventional software program. In fact, the claim does not require that even the best poses are selected nor does the claim require the selected poses to be utilized in anyway.

The claims are also different from the claims in *Diamond v. Diehr*, 450 U.S. 175 (1981) ("*Diehr*") which were found to be patent eligible. In *Diehr*, the claims were directed to a method of operating a rubber-molding press of precision molded compounds. *Id.* at 179, fn. 5 (reproducing claims 1, 2, and 11). The temperature in the mold during the rubber-molding process was constantly determined and provided to a digital computer. *Id.* The computer calculated the Arrhenius equation for the reaction time during the cure using the temperature and used the equation to determine when to open the press. *Id.*

Although the claim recited a mathematical algorithm, namely the Arrhenius equation, the Court held that the claim was eligible for a patent.

> [W]hen a claim containing a mathematical formula implements or applies that formula in a structure or process which, when considered as a whole, is performing a function which the patent laws were designed to protect (e. g., transforming or reducing an article to a different state or thing), then the claim satisfies the requirements of § 101

Diehr, 450 U.S. at 192. The Court emphasized that the process in *Diehr* was to make rubber, and the mathematical formula was simply used to determine when to *open* the mold so over curing did not occur. *Id.* at 1057. In this case, the claimed steps of providing poses, clustering, and selecting based on interaction energies do not involve a change in how the process is carried as it did in *Diehr* (i.e., opening the mold). The steps enable poses to be selected, but there is no requirement in the claim that selected poses are used for a particular purpose or even that the best poses are selected. Indeed, it is not even clear whether poses based on only phobic or polar interaction energies would be better than poses based on total interaction energy as required by the claims. The claim merely selects poses based on phobic and polar interaction energies, but does not contain a step in which these poses are used or combined with the total interaction energy. Rather, the steps involve merely the collection of data without any application of it.

The claims are also not directed to an improvement in computer functionality as in *Enfish, LLC v. Microsoft Corp.*, 822 F.3d 1327, 1335–36 (Fed. Cir. 2016), where a basis for patent eligibility was found.

In sum, we conclude that the claims are directed to a patent ineligible concept.

While we agree with the Examiner that the claim is directed to an abstract idea, we further note that the claim is also directed to an ineligible natural law or phenomenon because it merely informs the relevant audience of the factors that affect the molecular poses between a naturally-occurring binding molecule and target, namely factors that affect the native conformation of a ligand or substrate bound to naturally occurring protein. *See, e.g.*, Itai ¶¶ 121, 122, 127, 137 (Example 2) (describing the binding mode of naturally-occurring dihydrofolate reductase and its substrate). As held in *Mayo Collaborative Services v. Prometheus Laboratories, Inc.*, 132 S .Ct. 1289, 1297 (2012), a patent which simply describes a relation that "exists in principle apart from any human action," namely, the binding between a naturally-occurring protein and its ligand or substrate, is a natural law and patent ineligible subject matter. Consistently, Appellants characterize the claims as "**representative of physical properties of objects** (molecules)." Appeal Br. 10. The properties of a molecule are naturally-occurring and thus encompass a natural phenomenon, falling within the judicial exception to patent eligibility.

Appellants contend that the claims are more than just "data manipulation" because they simulate physical systems. Appeal Br. 9. However, simply because the data is a representation of a physical molecule does not exclude it from being an abstract idea because none of the steps are tied to the physical molecule, itself, or interact in any way with the physical molecule or a process of manipulating it.

The second step of the patent eligibility analysis requires a determination of whether the claims do significantly more than simply describe the abstract idea or natural law. *Mayo*, 132 S. Ct. at 1297. The

claim limitations must be scrutinized to determine whether the claims contain an "inventive concept" to "transform" the claim into patent-eligible subject matter. *Alice*, 134 S. Ct. at 2357 (quoting *Mayo*, 132 S. Ct. at 1298).

> The transformation of an abstract idea into patent-eligible subject matter "requires more than simply stat[ing] the [abstract idea] while adding the words 'apply it.'" *Id.* (quoting *Mayo*, 132 S.Ct. at 1294) (alterations in original). "A claim that recites an abstract idea must include 'additional feature' to ensure 'that the [claim] is more than a drafting effort designed to monopolize the [abstract idea].'" *Id.* (quoting *Mayo*, 132 S.Ct. at 1297) (alterations in original). Those "additional features" must be more than "well-understood, routine, conventional activity." *Mayo*, 132 S. Ct. at 1298.

Ultramercial, Inc. v. Hulu, LLC, 772 F.3d 709, 715 (Fed. Cir. 2014).

As discussed in connection with the rejection based on obviousness, the steps of providing molecular poses, clustering the poses into families, and utilizing total energy interactions to select poses was "well-understood, routine, conventional activity" as established by the teachings of Cho relied upon by the Examiner in the obviousness rejection. Final Act. 6–7. The additional steps of selecting poses individually based only on polar and phobic interactions involve the same conventional step of selecting energy interactions as described in Cho, Itai, and McConkey. We fail to see any technical improvement embodied by the claim, particularly when it was known in the prior art to select poses based on total interaction energy. Appellants did not provide evidence that such selection steps based on polar and phobic energy interactions alone provided better pose selection or operate in an unconventional manner. *Amdocs*, 841 F.3d at 1300–01.

Appellants also contend that the claims do not preempt an abstract idea. Appeal Br. 12. However, as discussed in *Ariosa Diagnostics, Inc. v.*

Sequenom, Inc., 788 F.3d 1371 (2015), 1379, "[w]hile preemption may signal patent ineligible subject matter, the absence of complete preemption does not demonstrate patent eligibility." Moreover, *Ariosa* held: "Where a patent's claims are deemed only to disclose patent ineligible subject matter under the *Mayo* framework, as they are in this case, preemption concerns are fully addressed and made moot." Consequently, since the claimed subject matter is ineligible under *Mayo*, we need not address the preemption concern.

SUMMARY

For the foregoing reasons, the obviousness rejections (Rejections 1 and 2), and the 101 rejection (Rejection 3) are affirmed.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a)(1)(iv).

AFFIRMED